There is little information on the magnitude and pattern of human exposures to endocrine disruptors. The limited exposure data that exist are primarily for various environmental media, such as chemical concentrations in air, food, and water. Often these data are limited by geographical regions and cannot be extrapolated to national trends. More relevant measures of human exposure, such as chemical concentrations in human blood, breast milk, and human tissue, are rare. Often these data are available only for high exposure areas and populations. As chemicals suspected of contributing to endocrine disruption in humans are identified, it will be necessary to obtain high-quality exposure data to perform human risk assessments. Each major state of the science report on endocrine disruptors has acknowledged the critical need for research to increase our understanding of human exposures and related health outcomes.

The human health issue regarding exposure to endocrine disruptors primarily relates to: (1) adverse effects observed in fish and wildlife, (2) the increased incidence of specific endocrine-related adverse human health outcomes/diseases, and (3) observations of endocrine disruption in well-conducted experiments involving laboratory animals. These chemicals can affect the endocrine system in several ways including interfering with hormone synthesis and release from the endocrine gland, competing with the hormone for the binding sites on transport proteins in the blood, binding to the receptor to either block hormone action or mimic it, and producing changes in hormone metabolism and elimination (IPCS, 2002).

There are a few clear examples of adverse human health effects following high exposures to environmental chemicals (e.g., accidental releases or poisoning incidents). Analysis of the human data by itself has not provided firm evidence of direct causal associations between low level exposure to endocrine-disrupting chemicals and adverse human health outcomes.

Of particular interest is exposure during very early development, both *in utero* and postnatally. Sexual differentiation, growth, and development are under hormonal control. Many of these early processes are unique to this time period and disruptions of carefully timed processes may lead to irreversible adverse human health outcomes. Interest has focused on: (1) adverse effects on reproductive and sexual development and function, (2) altered immune system, nervous system, and thyroid development and function, and (3) cancers of various endocrine-sensitive tissues including the testes, breast, and prostate. Additional research is needed to determine whether linkages exist between these adverse human health outcomes/diseases and exposure to suspected endocrine disruptors. However, this research is challenging as the manifestation of the condition is frequently not observed until years after exposure has occurred and the measured concentration of the chemicals in the affected adult may be very different from in utero, neonatal, or pre-pubertal exposures/concentrations that may have given rise to the adverse outcome.

4.5 Assessing the Environmental Burden of Disease

Many factors may cause or influence disease in humans. These factors include heredity, social factors, dietary factors, and environmental factors (e.g., chemical pollutants, infectious microorganisms, and radiation). The extent to which environmental factors influence overall disease is not entirely understood. Disease burden, global burden of disease, and environmental burden of disease are concepts used to express the burden of disease on society:

- **Disease burden** is the effect on society of both disease-related mortality and disease-related morbidity (Kay, 2000; WHO, 2002). It is assessed by several health measures, including mortality rates, morbidity rates, and the number of days in the hospital. Historically, disease burden has been investigated by analyzing disease outcomes, such as cancer, rather than analyzing risk factors that may cause cancer or disease in general. For example, it is easier to compare cancer incidence between two countries than to compare risk factors of cancer; ionizing radiation may be the major risk factor for cancer in country A, while dioxin may be the major risk factor in country B.
- **Global burden of disease (GBD)** assesses the disease burden on a worldwide basis and then apportions that burden to various causes, such as genetic, behavioral, and environmental.
- **Environmental burden of disease (EBD)** measures that portion of the GBD which is due solely to environmental risk factors.

EBD provides a method for summarizing the environmental health of populations. The summary health data collected from EBD measurements help identify environmental risk factors with significant public health implications. EBD data can also be used to help prioritize funding allocations for health and environmental research, assist in environmental policy development, justify environmental advocacy, assess the cost-effectiveness of interventions, and monitor the progress of a population's health (Prüss, et al., 2001). More important, EBD provides a way to normalize risk factors, allowing comparable health evaluations between populations. Two approaches are commonly used to determine the degree of disease burden that stems from environmental risk factors:

- The **outcome-based approach** determines the degree to which specific environmental risk factors cause a disease relative to other environmental risk factors.

- The **exposure-based approach** assesses the adverse health outcomes resulting from dose-response relationships between risk factors and associated disease outcomes (Prüss, et al., 2001).

This section summarizes estimates, in different studies, of the environmental burden of disease.

World Health Organization Evaluation

In 1998, WHO estimated that 23 percent of GBD is due to environmental hazards, including occupational exposures (WRI, et al., 1998). In 1999, WHO researchers and researchers from the University of California reported that an estimated 25 to 30 percent of the GBD was attributable to the environment (Smith, et al., 1999).

In 2000, WHO introduced a new methodology for evaluating changes to EBD, termed comparative risk assessment (CRA). CRA measures the GBD due to risk factors. WHO is currently developing CRA guidelines to help countries and smaller population groups, such as villages and towns, measure their respective EBD (Kay, 2000). CRA does not have one standard unit, however, and it incorporates other methodologies used to assess EBD. Because of this variability in assessment methodologies, comparing EBD for different countries can be difficult. Further, because EBD has not been quantified extensively in the U.S., this country's level of EBD cannot be easily compared with that of the rest of the world.

Doll and Peto Estimates

Richard Doll and Richard Peto quantified the environmental contribution to disease in their 1981 landmark study *The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today.* In that study, they concluded that pollutants in air, water, and food contributed from 2 to 5 percent to cancer mortality (Doll and Peto, 1981). They quantified the portion of cancer deaths that were attributable to various environmental causes, excluding tobacco smoke (Exhibit 4-40). Thirty percent of cancer was ascribed to tobacco use.

Other Estimates

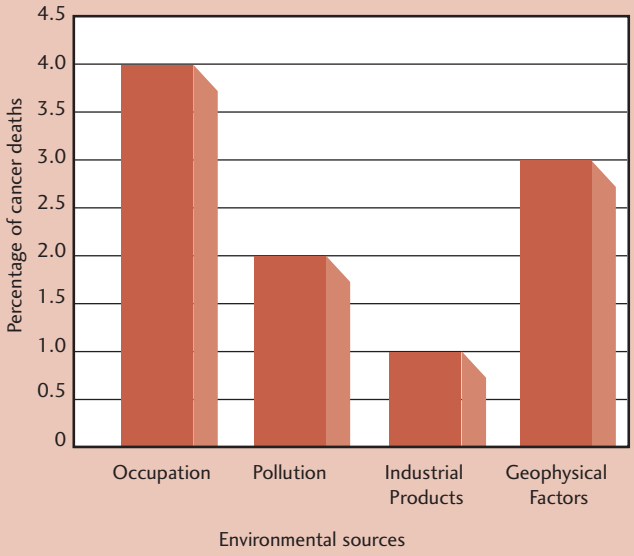
Other studies of EBD have investigated specific environmental risk factors and disease outcomes. For example, Wynder and Gori concluded in 1972 that environmental factors caused 12 percent of all cancer cases for men and 14 percent for women in the U.S. (Doll and Peto, 1981).

Why EBD Estimates Differ

EBD estimates are affected by the definition of "environment" that is used in making the determination (Smith, et al., 1999), as well as the measurement unit used, such as reporting mortality as a percentage of the population. For example, some researchers include factors such as stress or injury as environmental causes of disease, while others include stress and injury as social causes of disease.

The quantity of disease burden (such as disease outcome or risk factors) measured in EBD studies also produces variation in EBD estimates. These differences can be attributed to the different ways that risk factors are categorized, or to differences in the amount of disease burden attributed to a particular source.

Exhibit 4-40: Estimated proportions of cancer deaths in the United States attributed to selected environmental factors



Note: Tobacco is not included in this table. There was not a distinction between environmental tobacco smoke and mainstream smoke.

Source: Doll, Richard and Richard Peto. *The Causes of Cancer: Quanitative Estimates of Avoidable Risks of Cancer in the United States Today.* 1981.